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Acute Myocarditis Following mRNA-1273 SARS-CoV-2 Vaccination

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Title: Acute Myocarditis Following mRNA-1273 SARS-CoV-2 Vaccination

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Brief Summary:

We present a case of acute myocarditis in a young, healthy male after his second dose of the mRNA-1273 SARS-CoV-2 (Moderna) vaccine. The aim of this report is to highlight and raise awareness of a potential rare side effect of this vaccine that has not yet been described in the literature.

Abstract:

Myocarditis has previously been described as a rare side effect of both influenza and smallpox vaccines. In this report, we present a case of acute perimyocarditis in a young, healthy male after vaccination with the mRNA-1273 SARS-CoV-2 (Moderna) vaccine. He presented with chest pain and decompensated heart failure 3 days after administration of his second dose, and his symptoms resolved by 9 days post-inoculation. This case highlights a potentially rare but serious side effect of this mRNA vaccine that primary care physicians and cardiologists should be aware of in order to identify and appropriately manage these patients.

Clinical Presentation:

A 34-year-old previously healthy male presented to the hospital with a 3-day history of fevers and myalgias and 2-day history of a dull, retrosternal chest pain that was both positional and pleuritic nature. He had received his second dose of the mRNA-1273 SARS-CoV-2 (Moderna) vaccine one day prior to his symptom onset. He took no medications, did not use any recreational drugs, and his infectious review of systems was otherwise negative.

On physical exam, he was febrile (39.1^{o}C), tachycardic with a HR of 102, blood pressure of 103/67 and tachypneic with a respiratory rate of 28 and oxygen saturation of 93% on room air. Jugular venous pressure was elevated, he had no murmurs or rubs, and he had mild crackles to lung bases. Electrocardiography showed lateral PR depression and ST elevation mirrored in aVR with PR elevation and ST depression (Figure 1). Laboratory investigation on admission showed high-sensitive troponin T (hs-cTnT) concentration of 4026 ng/L (normal < 14 ng/L) which peaked at 5203 ng/L, NT-proBNP 1551 ng/L (normal < 125 ng/L), white blood cell count 8.4 x 10^{9}/L, lactate 1.1 mmol/L, and C-reactive protein 111 mg/L. Sputum and blood cultures were negative and nasopharyngeal COVID-19 polymerase chain reaction was non-reactive. Chest X-ray revealed mild pulmonary edema. His symptoms, physical exam and investigations were suspicious for perimyocarditis.

A transthoracic echocardiogram revealed reduced left ventricular ejection fraction (LVEF) of 43% without pericardial effusion (see supplementary material videos 1-4). A cardiac MRI performed on day 4 of admission showed normalization of the LVEF to 54% with subepicardial late gadolinium enhancement in the anterolateral and inferolateral segments, as well as patchy myocardial edema on T2 weighted images (Figure 2), meeting the Lake Louise criteria for myocarditis. The MRI also demonstrated pericardial enhancement consistent with inflammation, confirming the clinical suspicion of perimyocarditis. By day 5 of his admission, his symptoms had resolved and his hs-cTnT and CRP improved to 59 ng/L and 20 mg/L respectively. Given his clinical, biochemical and LVEF improvement, an endomyocardial biopsy was deferred. He was discharged from the hospital symptom free on medical therapy with high dose aspirin, colchicine, bisoprolol and rampiril with a plan for close outpatient follow up.

Discussion:

Myocarditis is an acute inflammatory disease of the myocardium predominantly associated with infectious agents (often viruses), toxic substances or systemic immune-mediated disorders. The gold standard for diagnosis is via histopathological sampling with endomyocardial biopsy, however, this is not always feasible or practical. A probable diagnosis can be achieved in the appropriate clinical context with elevated cardiac enzymes as well as functional and structural abnormalities on cardiac echocardiogram and MRI [1].

Vaccine related myocarditis is rare but has been documented with live-attenuated influenza and small-pox vaccines [2-3]. The causality is uncertain, and mechanism is not fully understood, but there are some hypotheses that post-vaccine myopericarditis may be secondary to lymphocytic infiltration resulting in an immune mediated myocardial injury [3].

COVID-19 Vaccine mRNA-1273 developed by ModernaTx, Inc is a pre-fusion SARS-CoV-2 spike glycoprotein (S) antigen encoded in mRNA and formulated in lipid nanoparticles, representing a novel vaccination technology with ongoing surveillance for potential unrecognized side-effects. During the phase 3 study for this vaccine, no cases of myocarditis were documented in any of the 30,420 participants [4].

Cardiac involvement in COVID-19 infection is well recognized, with manifestations ranging from myocardial injury to cardiogenic shock. Myocarditis itself is a known complication of coronavirus disease [5]. With the global vaccination effort well underway and millions of mRNA vaccines administered, the potential for myocarditis after vaccination is being increasingly recognized in case series [6-7]. Similar to our patient, most reported cases describe younger male patients presenting within days of their second vaccine dose who have a self-limited course without malignant arrythmias or need for advanced circulatory support [6-7]. While this patient and others reported thus far have had a favourable course and outcome, recognition of this entity

is important in managing these patients appropriately, and may have yet unknown future implications. The purpose of this case is to highlight a potential rare side effect of this vaccine for clinicians to be aware of, and not to deter clinicians and patients from the proven efficacy and overall safety profile of this mRNA vaccine.

Novel Teaching Points:

- Clinicians should be aware that patients presenting with chest pain after vaccination with mRNA vaccines (Moderna or Pfizer-BioNTech) may have myocarditis or perimyocarditis
- The natural history of mRNA vaccine associated myocarditis is not known, but case reports suggest a favourable prognosis and rapid recovery
- Myocarditis after mRNA vaccination appears to be rare, and the goal of this report is not to deter clinicians or patients from vaccination, but to raise awareness of this clinical entity

Disclosures
None

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Figure 1. 12-lead electrocardiogram obtained on presentation shows ST elevation in I, aVL, V4-V6 with PR elevation and ST depression in aVR.

Figure 2. A) Four-chamber FIESTA sequence in diastole demonstrating normal indexed cardiac chamber sizes (LV EDV 153 mL, RV EDV 167 mL) and no pericardial effusion. B) Short axis oblique (SAO) triple inversion recovery (TIR) sequence at the level of the mid-LV demonstrating patchy myocardial edema (asterix). C) and D) SAO late gadolinium enhancement inversion recovery sequence (TI = 260 ms) demonstrating pericardial enhancement (arrowheads) and subepicardial late gadolinium enhancement (LGE) in the mid LV anterolateral and inferolateral segments (arrows).

Supplementary Video 1. Parasternal long axis view showing infero-lateral wall hypokinesis.

Supplementary Video 2. Parasternal short axis view showing infero-lateral hypokinesis.

Supplementary Video 3. Apical 4-chamber view showing antero-lateral wall hypokinesis.

Supplementary Video 4. Apical 2 chamber view showing inferior wall hypokinesis. Ejection fraction 43% by Simpson's Method.